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Bioterrorism Agent Fact Sheet

Botulism/*Clostridium botulinum*

Disease

Botulism is a rare disease caused by ingestion of the anaerobic, spore-forming bacillus, *Clostridium botulinum*. Botulism neurotoxins are the most potent toxins known to man. There are three forms of naturally occurring botulism: foodborne, wound and infant (intestinal), and one man-made form: inhalational. The inhalational form is the most likely to be used in a bioterrorism attack, although dissemination through contaminated food could also occur. A thorough history may help differentiate the mode of attack; if no common food source is identified during an outbreak, bioterrorism should be suspected and an investigation should be initiated to determine the common site of aerosolization release.

Inhalational: Does not generally occur naturally, but has been demonstrated in lab settings with primates; a few cases of accidental human transmission have been documented in veterinarians

Food-borne: Most common form of the disease worldwide. Results from ingestion of food contaminated with organisms that have produced the preformed toxin; Case fatality rate: 7.5%

Wound: Rare form of the disease. Results from introduction of *c botulinum* into a wound; historically occurred during wartime when soil often contaminated wounds, but more recently it develops in skin abscesses or in traumatized tissue; Case fatality rate: 12.5%

Infant (intestinal): Most frequent form of disease in the US. Primarily occurs in infants as a result of intestinal colonization following ingestion of spores; honey has been implicated as a possible factor. > 90% of cases occur in children ≤ 6 months of age; Case fatality rate: < 1%

Diagnosis

A single case of known or suspected botulism constitutes a public health emergency and should be immediately investigated as a potential foodborne outbreak or bioterrorism event. Presumptive diagnosis should be made based on signs and symptoms; laboratory confirmation should be obtained for definitive diagnosis. It is imperative to obtain a history focusing on food intake and potential exposure to the organism.

Patients present like those with tetanus, myasthenia gravis or Guillain-Barre Syndrome. Differentiating symptoms in botulism include: disproportionate amount of palsies caused by cranial nerve damage, more hypotonia in facial muscles than in muscles below the neck, and the lack of sensory changes that usually accompany other disorders that result in flaccid paralysis.

Confirmation testing includes detection of toxin through mouse bioassay using the following patient lab specimen(s): foodborne (blood and stool), wound (blood and wound) and intestinal (stool). In order for the bioassay to be accurate, all specimens should be refrigerated during storage, serum samples should be obtained before initiation of treatment with antitoxins, and the lab should be notified if the patient has taken anticholinesterase medications. Definitive diagnosis may be made through monovalent and polyvalent diagnostic antitoxins available from the CDC and a limited number of public health departments. Stool and gastric samples may help identify a bioterrorism attack by ruling out naturally occurring disease and diagnosing inhalational botulism.

Botulism

Clinical Features of Botulism

Incubation period varies according to the types of botulism and the extent of exposure to the toxin:

Inhalational: onset was approximately 72 hrs in the three known inhalational cases and monkeys developed disease 12-18 hrs after exposure in lab studies, but the true incubation period for aerosolized botulism is unknown

Food-borne: 12-36 hrs (range 6 hrs - 10 days) 12-72 hrs

Wound: 7.5 days (range: 4-18 days) after the injury

Botulism toxin causes permanent nerve damage by binding to nerve synapses and therefore interfering with the release of acetylcholine. Botulism toxin cannot cross the blood-brain barrier and does not affect the central nervous system. Sensory systems remain intact while the peripheral cholinergic synapses are damaged, resulting in flaccid paralysis yet the patient remains mentally alert and afebrile. The toxin first affects the muscles connected to the cranial nerves.

Early symptoms of all forms of the disease include double or blurred vision, difficulty with speaking and swallowing, dry mouth, and fatigue. As the disease progresses, symmetrical muscle weakness develops starting at the trunk and descending to the extremities; deep tendon reflexes generally remain intact. Mental functioning generally remains intact unless secondary complications develop. Death often results when the toxin attacks the respiratory system resulting in airway obstruction and respiratory paralysis. Recovery may occur if paralyzed muscles are reinnervated, but this process may require weeks to months and intensive supportive therapy is required throughout this period of recovery.

Foodborne: Initial symptoms include vomiting, constipation, GI upset and, rarely, diarrhea, followed by symptoms listed above that result from cranial nerve damage. These GI symptoms are postulated to be caused by other components in the food and not the botulism toxins; therefore, a bioterrorism attack

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Treatment

Rapid diagnosis and initiation of treatment and supportive care provide the best opportunity for survival. Treatment should be initiated as soon as the diagnosis is suspected; do not wait for lab confirmation. Antitoxin, available from the CDC, should be administered to all patients with known or suspected disease. Antitoxin cannot reverse affects of toxin that has bound to nerve receptors (ie, there will not be an improvement of clinical symptoms), but it does prevent further progression of nerve damage. Because the antitoxin is generally derived from horse serum, serious complications (including anaphylaxis and serum sickness) may develop. Supportive care generally includes intensive care, tube feedings or TPN, and placement on a ventilator (in 29% of foodborne cases and > 60% of infant cases).

Recommendations for safe and effective administration of antitoxin have changed over time; package insert materials should be reviewed before initiation.

Foodborne and inhalational botulism:

Adults: Administer one vial (5500-8500 IU of each type-specific antitoxin) trivalent botulism antitoxin IV diluted 1:10 in 0.9% saline solution; patient's serum should be retested after treatment to ensure that all toxin has been neutralized.

Children: Same as adults • Reverse Trendelenburg (20-25º) with support of the cervical spine for infants not on a ventilator

Infant botulism: Supportive care only • do not administer antitoxin; use has been shown to result in adverse reactions and most patients recover well without treatment

Non-effective therapies: Aminoglycosides and clindamycin should not be given as they may worsen paralysis by reacting with the botulism at the site of the neuromuscular junction. Antibiotics should be avoided in patients with infant botulism; increased toxin release may result from bacterial cell lysis following treatment.

Post-Exposure Prophylaxis

Antibodies to botulism or the administration of antitoxin would be sufficient to prevent disease following exposure to botulism. However, because of limited supplies and potential severe side effects, antitoxin use is not recommended except for those patients that are exhibiting symptoms. Everyone that is known or suspected of having been exposed should be closely monitored and treated with antitoxin at the first sign of disease.

Vaccination

There is currently no vaccine available for the general public. Laboratory employees who work with the toxin or botulism organisms and military employees that are at risk for exposure may be eligible to receive a pentavalent toxoid vaccination through the CDC.

Decontamination

C botulinum is a hardy spore that is highly heat-resistant, but botulism toxin in food is easily destroyed through the normal cooking process (heating ≥ 85º C for 5 minutes). Weather conditions and size of the aerosolized particles determine how long the toxin can remain airborne, but it is estimated that the majority of the toxin will be inactive within 2 days of release. If a warning is issued before a release, some protection can be achieved by covering the mouth with cloth or a mask; botulism may be absorbed through mucous membranes, but cannot penetrate intact skin. Following a known exposure, patients and their clothing should be washed with soap and water. Surfaces exposed to the initial release should be cleaned with a 1:10 hypochlorite (bleach) solution.

Additional information and references available at www.bioterrorism.slu.edu

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involving a purified form of botulism dispersed in food may not result in GI symptoms in the victims. Between 57-81% of pts require respiratory support, which may include ICU admission and insertion of an ET-tube or tracheostomy.

Wound: Form of the disease that most closely resembles tetanus. Neurotoxins produced by the contaminating organisms in the affected wound disseminate throughout the body and destroy the nerve endings. Symptoms are similar to foodborne illness except for GI symptoms.

Infants: Disease results from GI absorption of toxin following colonization; method of colonization and toxin absorption is currently unknown. The initial symptom is generally constipation, although it is often accompanied by lethargy, lack of appetite, drooling, and weakness. This is followed by descending symmetrical paralysis evidenced by bulbar palsies: poor head and muscle control, flat affect, ptosis, impaired gag, suck and swallow reflexes, dilated or sluggish pupil reaction, and a weak cry. "Floppy baby syndrome" (hypotonia, loss of head control and overall weakness) often develops over the following few days. Respiratory failure is common; intubation is required in over 80% of cases and ventilatory support is necessary.

Infection Control

Only standard precautions are necessary unless the patient is suspected of having flaccid paralysis as a result of meningitis (Respiratory Precautions). Human to human transmission does not occur.

Reporting

Report known or suspected cases or suspected intentional release of botulism immediately to your local health department and hospital epidemiologist. The local health department is responsible for notifying the state health department, FBI, and local law enforcement. The state health department will notify the CDC.

Disclaimer

Information contained in this fact sheet was current as of August 2001, and was designed for educational purposes only. Medication information should always be researched and verified before initiation of patient treatment.

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